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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| EXAMINER | |
|---|---|
| HENLEY III, RAYMOND J | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1614 | |

DATE MAILED: 07/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/694,001 | SCHOLKENS ET AL. | |
| | Examiner | Art Unit | |
| | Raymond J Henley III | 1614 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *14 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *16-70* is/are pending in the application.

4a) Of the above claim(s) *19,29 and 35-70* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-18,20-28 and 30-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/28/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

**CLAIMS 16-70 ARE PRESENTED FOR EXAMINATION**

Applicants' Response filed June 24, 2004, Preliminary Amendment and Information Disclosure Statement filed October 28, 2003 and May 19, 2004 have been received and entered into the application. Accordingly, the specification at page 1 has been amended, claims 1-15 have been canceled and claims 16-70 have been added. Also, as reflected by the attached, completed copies of form PTO-1449, the cited references have been considered.

***Restriction Requirement***

As per the Restriction Requirement set forth in the previous Office action, applicants have elected, with traverse, the invention of Group 1, claims 16-35 wherein further election of myocardial infarction as the cardiovascular event, an ACE inhibitor as the inhibitor of the renin-angiotensin system and a cholesterol lowering agent being additionally administered was made.

Applicants have traversed this requirement based on their opinion that a search for all of the subject matter of claims 16-70 would not present an undue burden to the Examiner. However, insofar as each grouped invention is directed to a different therapeutic objective and thus would require separate therapeutic considerations as well as a search in the prior art consistent with not only such objectives, but with each of the possible combinations of active agents employed, the Examiner cannot agree. Accordingly, for the reasons of record, the requirement for restriction is hereby made **FINAL**.

Based upon not only applicants' election of Group I, but also the species election, claims 19, 29 and 35-70 are withdrawn from further consideration as being drawn to non-elected subject matter. See 37 CFR 1.142.

Claims 16-18, 20-28 and 30-34 are herein acted upon the merits.

***Specification***

The disclosure is objected to because of the following informality,

At page 1 of the specification, line 2, "now abandoned" should be inserted after "2000" in order to update the status of the parent application.

Appropriate correction is required.

***Claim Rejection - 35 USC § 112, First Paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 16-18, 20-28 and 30-34 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the reduction of the risk of a cardiovascular event in a patient does not reasonably provide enablement for the prevention of such a risk. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The burden of enabling the preventing the risk of a cardiovascular event would be much greater than that of enabling the treatment of such diseases. In the instant case, the specification does not provide guidance as to how one skilled in the art would accomplish the objective of preventing of such risk or how a patient could be kept from ever being susceptible the risk of a cardiovascular event. Nor is there any guidance provided as to a specific protocol to be utilized in order to show the efficacy of the presently claimed active ingredients for preventing the risk of a cardiovascular event.

Specifically, it is highly unlikely, and the Office would require experimental evidence to support the contention that the claim specified actives could actually prevent the risk of a cardiovascular event by simply administering, by any method, an amount of the claim specified active agents. The specification fails to enable one of ordinary skill in the art to practice the presently claimed method for preventing the risk of a cardiovascular event.

The term "prevention" or "preventing" is synonymous with the term "curing" and both circumscribe methods of treatment having absolute success. Since absolute success is not reasonably possible with most diseases/disorders, especially those having etiologies and pathophysiological manifestations which are as complex/poorly understood as cardiovascular diseases, the specification is viewed as lacking an adequate written description of the where the risk for a cardiovascular event may be actually prevented.

### *Claim Rejection - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 16-18, 20-28 and 30-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Olukotun et al. (U.S. Patent No. 5,622,985, cited by the Examiner) in view of the Merck Manual (cited by the Examiner) and Applicants' acknowledgment at page 6, last paragraph – page 7, second full paragraph of the present specification.

Olukotun et al. teach a method of preventing or reducing the risk of a second heart attack, i.e., myocardial infarction/cardiac arrest, which comprises administering to a patient in need thereof a combination of an statin-type cholesterol lowering drug which may be pravastatin, lovastatin or simvistatin (see the abstract and col. 3, lines 26 and 29 and col. 8, line 26) in combination with an angiotensin converting enzyme inhibitor (ACE inhibitor) in general and of which the following are specifically taught: captopril (col. 6, line 66), enalapril (col. 7, line 27), fosinopril (col. 7, line 33), alacepril (col. 7, line 47), ramipril (col. 7, line 48), cilazapril (col. 7, line 51), lisinopril (col. 7, line 54), deapril (col. 7, line 56), spirapril (col. 7, line 58), perindopril (col. 7, line 60) and quinapril (col. 7, line 61). A non-hypertensive patient is also taught (col. 3, line 7).

The differences between the above and the claimed subject matter lie in that Olukotun et al. fail to teach:

(1) The patient risk factors, presence of diabetes or age as in present claims 20-23 and 25; and

(2) Each of the claimed ACE inhibitors.

However, the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains because:

(1) The patient population of Olukotun et al. are those who have already suffered a myocardial infarction and would not be unreasonable to expect that such people would continue to suffer from risk factors predisposing them to a second myocardial infarction. Indeed, the objective of Olukotun et al. is to reduce the risk of a second heart attack thus implying that the patients do indeed have risk factors for having another heart attack. Specific risk factors for heart attacks were well known such as coronary artery disease (Merck at page 488, first paragraph) and cigarette smoking. Also, the patient population of Olukotun et al. is limited neither to having or not having additional disease states such as diabetes nor to a specific age group. Thus, that the patient of Olukotun et al. may be also suffering from diabetes or be 55 years of age is not outside the scope of their disclosure.

(2) Olukotun et al. teach ACE inhibitors in general and the selection of any specific ACE inhibitors from those known, such as those acknowledged by applicants at page 6, last paragraph – page 7, second full paragraph, would have been a matter well within the purview of the skilled artisan.

Accordingly, for the above reasons, the claims are deemed properly rejected and none are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Raymond J Henley III whose telephone number is 571-272-0575. The examiner can normally be reached on M-F, 8:30 am to 4:00 pm Eastern Time.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Raymond J Henley III
Primary Examiner
Art Unit 1614

July 7, 2004